SHORT COMMUNICATION

Association of mortality and phase angle measured by different bioelectrical impedance analysis (BIA) devices

Laurence Genton[1], François. R. Herrmann[2], Adrian Spörri[3], Christophe E. Graf [4]

[1] Clinical Nutrition, University Hospitals of Geneva, Switzerland

[2] Geriatrics, Dept. Internal Medicine, Rehabilitation and Geriatrics, University Hospitals of Geneva, Switzerland

[3] Social and Preventive Medicine, University of Bern, Switzerland

[4] Rehabilitation and palliative Care, University Hospitals of Geneva, Switzerland

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Abbreviations: BIA: bioelectrical impedance analysis. BMI: body mass index. CIRS: Cumulative Illness Rating Scale.

Correspondence:

Laurence Genton, Clinical Nutrition

Rue Gabrielle Perret-Gentil 4, Geneva University Hospitals, 1205 Geneva, Switzerland

Phone: +41 22 3729344 Fax: +41 22 3729363

E-mail: laurence.genton@hcuge.ch

Abstract

Purpose: A high phase angle measured by the Nutriguard® bioelectrical impedance analysis device is associated with a reduced mortality risk in older people. This retrospective study aims to analyze whether this association persists with the other devices that have been used in our hospital.

Methods: This study encompasses all people 65 yrs and older who underwent a phase angle measurement between 1990 and 2011 at the Geneva University Hospitals, with the RJL-101® (RJL Systems), Xitron 4000B® (Xitron Technologies), Eugedia® (Eugédia-Spengler) and Bio-Z® (Spengler). Diseases at the time of phase angle measurement were reported in the form of the Cumulative Illness Rating Scale. Date of death was retrieved until December 2012. Phase angle values were categorized into sex- and device-specific quartiles, where quartile 1 represents the lowest quartile and reference value. Cox regressions were performed to evaluate the association between phase angle quartiles and mortality.

Results: We considered 1878 people (969 women), of whom 1151 had died. In univariate sex-specific Cox regressions, the death risk decreased progressively as the phase angle quartile measured by the Bio-Z® or RJL-101® increased. The HR (95% CI) in quartile 4 was 0.36 (0.26, 0.50) and 0.38 (0.29, 052) in women and men measured with the Bio-Z® (both $p<0.001$), and 0.23 (0.14, 0.39) and 0.19 (0.10, 0.36) in women and men measured with the RJL-101® (both $p<0.001$). The association between phase angle and mortality persisted when adjusted for age, body mass index or co-morbidities. The small number of deaths in people who underwent a measurement by Eugedia® (n=93) or Xitron4000B® (n=56) did not allow performing multivariate Cox regressions.

Conclusions: Phase angle quartiles are associated with mortality in people aged >65 years when using the RJL-101® or Bio-Z device®.

Keywords: bioimpedance, older people, death

Introduction

An increasing interest arises in the potential of phase angle to predict adverse outcomes like mortality (1-3). Phase angle is a raw bioelectrical impedance analysis (BIA)-derived parameter which may reflect cell size, cell membrane integrity and/or the distribution of water in the extra- and intracellular compartments (4) (5). Mathematically, it can be obtained from the arctangent of the reactance to resistance ratio measured by BIA. Thus, phase angle values do not depend on equations and their inherent assumptions, in contrast to BIA-derived body composition, i.e. fat mass and fat-free mass.

In a recently published cohort study, we have included all people ≥ 65 yrs who had undergone a BIA measurement at the Geneva University Hospitals between 1990 and 2011 (n=3181) (6). Mortality was reported until December 2012. We have shown that the lower the phase angle quartile at the last BIA measurement performed with the Nutriguard® device (n=1307) (Data Input GmbH, Darmstadt, Germany), the higher was the death risk, independently of the co-morbidities (7). We had focused on the measurements performed with the Nutriguard® device because 1) this device is still used in our hospital, and 2) phase angle reference values using the same brand of BIA device have been published (8) and allowed us to standardize the values for age and body mass index (BMI).

However, we have not reported the association of mortality and the phase angle measured by the other BIA devices that we have used over the time span of 21 years. The rationale of performing additionally these analyses is that, in the absence of a gold standard, phase angle values likely differ between devices. This retrospective study aims to analyze whether phase angle values measured by the other BIA devices than the Nutriguard® are also associated with mortality.

Material and methods

We included the remaining 1878 people of our previously described cohort study (6), which encompassed all people ≥65 yrs who underwent a BIA measurement at the Geneva University Hospitals between 1990 and 2011. This study population included hospitalized and ambulatory patients followed in clinical routine by the nutrition unit, and healthy people recruited for research purpose in leisure clubs, the hospital staff, at fun runs and through advertisement in local newspapers. The proportion of hospitalized patients was about 50% (n=967). BIA measurements were performed at 50kHz and 0.8 mA, while the subject was lying in the supine position with electrodes placed on the right hand, wrist, angle and foot. The following devices were used: RJL-101® (1990 to 1995) (RJL Systems, Inc., Clinton Township MI, USA), Xitron 4000B® (1990 to 2011) (Xitron Technologies, San Diego, CA, USA), Eugedia® (1994 to 2000) (Eugédia-Spengler, Cachan, France) and Bio-Z® (1996 to 2002) (Spengler, Paris, France). All devices were calibrated for phase angle with a calibration jig (CJ 4000, Xitron Technologies, San Diego, CA, USA), before their use in our institution. A limit of ±2° for phase angle and ±5Ω for impedance was tolerated at 50 kHz. To test method agreement, we had measured the phase angle values of 8 healthy people with the RJL-101®, the Xitron®, and the Bio-Z®, without changing the position of the people nor the placement of the electrodes. Method agreement, calculated as the mean phase angle difference (2SD) obtained from the Bio-Z® minus the RJL-101® or the Xitron®, was -1.49° (0.45) and -1.50 (0.24), respectively. We also calculated fat-free mass with the Geneva formula (9), which was validated against DXA specifically in older persons (10). Fat mass was obtained by subtracting fat-free mass from body weight. Fat-free mass index and fat mass index were calculated as follows: fat-free mass or fat mass (kg)/body height $(m)^2$.

Date of death was considered until December 2012, and retrieved from the hospital computer database, the death registry of the state of Geneva and the Swiss National Cohort (11). We reported co-morbidities at the time of the BIA measurement in the form of the Cumulative Illness Rating Scale (CIRS) (12). It rates 14 systems and organs from 0 (healthy) to 4 (severe disease needing immediate intervention or hospitalization), and takes into account lifestyle modes as smoking and alcohol consumption. Its final score ranges from 0 (healthy) to 56 points.

Statistics

Results are shown as median (interquartile range) for continuous variables as they were not normally distributed according to Shapiro-Wilk tests. Comparisons between devices were performed with Kruskall-Wallis test.

Age, body mass index and CIRS were categorized like in our former study, because their distribution, tested by Shapiro-Wilks test, was not normal: age as 65-74 yrs, 75-84 yrs and ≥85 yrs, BMI as <18.5, 18.5-24.9, 25-29.9 and ≥30 kg/m^2 (13), and CIRS as quartiles of the population measured by the considered device. The association between mortality and device- and gender-specific phase angle quartiles were evaluated by univariate Cox regressions. We performed multivariate Cox regressions with adjustments for age (model 1), BMI (model 2) or CIRS categories (model 3) because we did not observe enough events to follow the rule of Harrel (14). This rule supposes a maximum of 1 variable for 10 events.

Results

The characteristics of the study subjects measured by the different BIA devices are shown in **table 1**. They were significantly different regarding age, body mass index, co-morbidities and phase angle.

The small number of deaths in women (n=16) and men (n=39) who underwent a BIA measurement by Xitron 4000B precluded the use of sex-specific phase angle quartiles in the Cox regressions. We thus focused on the three other devices (n=1683). In sex-specific univariate Cox regressions, the association between phase angle quartiles measured with the Bio-Z® and RJL-101® devices and mortality could be highlighted, although the cut-off quartiles differed between the BIA devices (**table 2**). No associatation between phase angle and mortality was observed when using the Eugedia® device. Sex-specific multivariate Cox regressions could be performed with the Bio-Z® and the RJL-101® device (**table 3**). They confirmed the findings of univariate Cox regressions even when adjusting for age, BMI or CIRS categories, i.e. the higher the phase angle quartile, the lower the death risk.

Discussion

This study shows that the mean phase angle values differed significantly between the subjects measured with the Bio-Z®, RJL-101®, Eugedia® and Xitron® devices. A low phase angle quartile was associated with a high death risk in people aged > 65 years, when using a Bio-Z® or a RJL-101® device. When adjusting for age, body mass index or disease, a low phase angle remained a risk factor of mortality.

The characteristics of the study population (age, BMI, diseases), or the technology itself may explain the differences in phase angle values between the devices. Reference values for phase angle are 7.7 and 10.5 % lower in the Swiss women and men (using several BIA brands cross-calibrated for resistance) (15), and 12.5 and 16% lower in the German women and men (using Data Input devices) (8) compared to the American population (using an RJL device) (16). Bosy-Westphal et al. reported that a discrepancy of 0.3° for phase angle may be related to differences between the Xitron® and Data Input devices, and that, although age and BMI influence phase angle values, they do not explain the differences between populations (8). This suggests that differences of phase angle values between our study groups may be related to different anthropometric characteristics, BIA devices or other unidentified factors. Thus, when evaluating the potential of a phase angle value on outcome at a population level, and in the absence of a gold standard for phase angle measurement, it is essential to use a single brand of BIA to avoid at least the confounding impact of different BIA devices.

Whether using an RJL-101® or a Bio-Z® device, a phase angle in the low quartile is associated with a high risk of mortality. This result confirms our previous findings using a Nutriguard® device but also other studies performed in older persons. A phase angle < 3.5°, measured by a Nutriguard® device at admission to a German hospital, increased the in-hospital mortality by four times (17). Similarly, a phase angle in the lowest quintile (women: 2.7-5.4°, men: 3.1-5.6°), measured by a Valhalla® device (Valhalla Scientific, San Diego, CA, USA), led to a two-fold increase of mortality risk at 12 years (18). The adjustment for BMI, age or CIRS did not change this association in our study. As a consequence, phase angle is associated with mortality independently of these other mortality risk factors.

This study could demonstrate the link of phase angle and mortality with the RJL-101® and the Bio-Z devices®, but has several limitations. It is not a population-based study and our subjects are likely more ill than the general population. However, the link between phase angle and mortality was confirmed when adjusting for co-morbidities and their severity. We did not use the different BIA devices in the same study population. This precludes the comparison of phase angle values. Finally, the number of events (i.e. deaths) was not high enough to make simultaneous adjustments for age, BMI and co-morbidities in the statistical analyses.

Future studies should evaluate differences in electrical parameters between commonly used BIA devices in large populations, in order to differentiate the variations related to devices vs. population characteristics. They should also better identify the factors which influence phase angle, especially in interventional studies with a longitudinal follow-up.

Conclusion

Phase angle quartiles are associated with mortality in people aged ≥ 65 years and older when using other BIA devices than the Nutriguard®, as the RJL-101® or the Bio-Z®, although the cut-offs of the phase angle quartiles differ.

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Statement of authorship

LG and CG designed the research; LG, FRH and CG analyzed data and performed statistical analysis; LG and CG wrote the paper; LG has the primary responsibility for final content.

Conflict of interest statement

None of the authors have any conflict of interest.

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Table 1: Baseline characteristics at the last BIA measurements (n=1683)

	Bio-Z®				RJL-101®				Eugédia®				p*
	N	%	median	IQR	N	%	median	IQR	N	%	median	IQR	
Women													
Age (yrs)	424	100	77.0	11.0	266	100	80.0.2	12.0	185	100	75.0	10.0	<0.001
Age at death (yrs)	301	71	83.4	12.8	150	56	87.0	9.0	89	48	87.6	10.4	<0.001
Length of follow-up (yrs)#	424	100	5.8	9.2	266	100	15.3	15.1	185	100	16.7	6.6	<0.001
Phase angle (degrees)	424	100	3.4	1.4	266	100	4.2	1.4	185	100	4.1	1.0	<0.001
Resistance (Ω)	424	100	577.2	146.6	266	100	602.0	143.0	185	100	558.9	88.0	<0.001
Reactance (Ω)	424	100	34.8	17.0	266	100	45.0	19.0	185	100	40.0	11.0	<0.001
Body mass index (kg/m^2)	424	100	24.2	7.5	266	100	23.7	5.6	185	100	26.6	6.4	<0.001
Fat mass index (kg/m^2)	424	100	9.3	5.1	266	100	8.6	3.6	185	100	10.5	4.0	<0.001
Fat-free mass index (kg/m^2)	424	100	14.8	3.5	266	100	14.8	2.4	185	100	16.0	3.0	<0.001
Cumulative Illness Rating Scale	393	93	10.0	8.0	154	58	5.0	5.0	114	62	3.0	5.0	<0.001
Men													
Age (yrs)	501	100	75.0	10.0	190	100	74.0	12.0	117	100	73.0	10.0	<0.001
Age at death (yrs)	397	79	78.9	10.8	106	56	82.5	12.7	53	45	83.5	11.2	<0.001
Length of follow-up (yrs)	501	100	3.4	8.8	190	100	14.7	17.4	117	100	17.1	9.4	<0.001
Phase angle (degrees)	501	100	3.7	1.7	190	100	4.9	1.8	117	100	4.6	1.7	<0.001
Resistance (Ω)	501	100	486.5	116.6	190	100	506.5	92.0	117	100	489.1	89.0	<0.001
Reactance (Ω)	501	100	30.8	13.7	190	100	42.0	17.0	117	100	39.2	10.6	<0.001
Body mass index (kg/m^2)	501	100	24.5	5.6	190	100	24.5	4.2	117	100	26.2	4.8	<0.001
Fat mass index (kg/m^2)	501	100	6.7	3.6	190	100	6.7	3.2	117	100	7.6	3.0	<0.001
Fat-free mass index (kg/m^2)	501	100	18.0	3.6	190	100	18.0	2.3	117	100	18.4	2.8	<0.001
Cumulative Illness Rating Scale	393	93	10.0	8.0	154	58	5.0	5.0	114	62	3.0	5.0	<0.001

IQR: interquartile range; # Time between the BIA measurements and death or censoring (31.12. 2011); * Comparisons between devices: Wilcoxon rank-sum U test

Table 2: Univariate Cox regression models evaluating the association of phase angles quartiles, measured by different BIA devices, and mortality.

	Women				Men			
	n	**Cut-off**	**HR**	**95% CI**	**n**	**Cut-off**	**HR**	**95% CI**
Bio-Z®	424				501			
Quartile 1	106	0.10-2.69	1.00	-	126	0.10-2.79	1.00	-
Quartile 2	106	2.70-3.39	0.63	0.47, 0.85	125	2.80-3.69	0.67	0.52, 0.88
Quartile 3	106	3.40-4.10	0.41	0.30, 0.57	125	3.70-4.50	0.54	0.42, 0.71
Quartile 4	106	4.10-7.40	0.36	0.26, 0.50	125	4.50-7.40	0.38	0.29, 0.51
RJL-101®	266				190			
Quartile 1	67	1.58-3.51	1.00	-	48	0.91-3.85	1.00	-
Quartile 2	66	3.52-4.18	0.78	0.52, 1.17	47	3.88-4.90	0.76	0.48, 1.20
Quartile 3	67	4.19-4.93	0.40	0.26, 0.62	48	4.91-5.60	0.36	0.21, 0.61
Quartile 4	66	4.94-11.64	0.23	0.14, 0.39	47	5.61-9.51	0.19	0.10, 0.36
Eugédia®	185				117			
Quartile 1	47	0.1-3.5	1.00	-	31	0.9-3.6	1.00	
Quartile 2	46	3.6-4.1	1.39	0.79, 2.42	28	3.7-4.5	0.91	0.42, 1.96
Quartile 3	46	4.1-4.6	0.69	0.37, 1.28	29	4.6-5.3	1.03	0.50, 2.14
Quartile 4	46	4.7-6.4	0.72	0.39, 1.32	29	5.4-7.7	0.76	0.35, 1.65

Table 3: Multivariate Cox regression models evaluating the association of phase angles quartiles, measured by different BIA devices, and mortality.

	Bio-Z®						**RJL-101®**					
	Women			**Men**			**Women**			**Men**		
	n	**HR**	**95% CI**	**n**	**HR**	**95% CI**	**n**	**HR**	**95% CI**	**n**	**HR**	**95% CI**
Model 1	424			501			266			190		
Quartile 1		1.00	-		1.00	-		1.00	-		1.00	-
Quartile 2		0.63	0.47, 0.85		0.67	0.52, 0.88		0.73	0.49, 1.11		0.68	0.42, 1.09
Quartile 3		0.41	0.30, 0.56		0.56	0.43, 0.73		0.36	0.23, 0.57		0.34	0.20, 0.59
Quartile 4		0.41	0.29, 0.57		0.41	0.30, 0.54		0.19	0.10, 0.34		0.16	0.08, 0.31
Model 2	424			501			266			190		
Quartile 1		1.00	-		1.00	-		1.00	-		1.00	-
Quartile 2		0.62	0.46, 0.85		0.70	0.53, 0.91		0.78	0.52, 1.18		0.75	0.47, 1.20
Quartile 3		0.40	0.29, 0.56		0.58	0.44, 0.76		0.41	0.26, 0.63		0.35	0.20, 0.62
Quartile 4		0.35	0.25, 0.49		0.42	0.31, 0.57		0.23	0.14, 0.39		0.19	0.10, 0.35
Model 3	393			481			154			107		
Quartile 1		1.00	-		1.00	-		1.00	-		1.00	-
Quartile 2		0.77	0.57, 1.04		0.71	0.54, 0.93		0.73	0.45, 1.19		0.67	0.40, 1.12
Quartile 3		0.55	0.39, 0.76		0.66	0.50, 0.87		0.42	0.25, 0.71		0.48	0.25, 0.91
Quartile 4		0.53	0.38, 0.75		0.51	0.38, 0.68		0.42	0.22, 0.77		0.36	0.16, 0.78

Model 1: adjusted for age category; model 2: adjusted for BMI category; model 3: adjusted for CIRS quartiles